**Mitosis and Cell Cycle Modeling (part II)**

**This activity is modified from an activity created by Lisa Brosnick, North Collins High School for the Biology-Chemistry Professional Development Network. Thank you Lisa for your creativity.** ☺

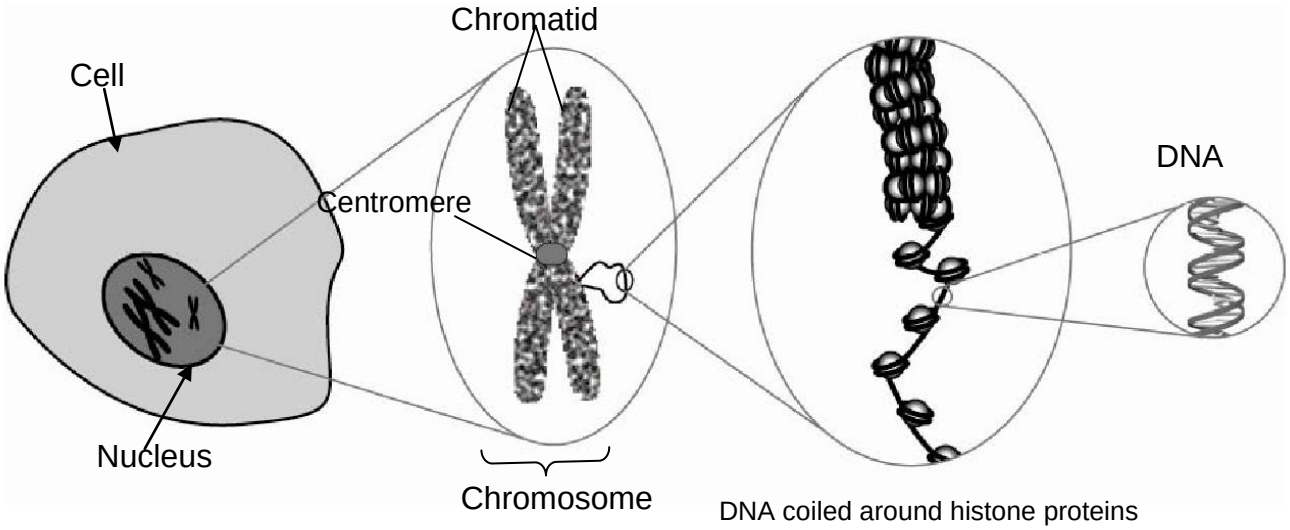
## Modeling the Normal Cell Cycle and Some Causes of Cancer

You will model the events and the controls of the cell cycle. Work in groups of 2-3 students. 50% of your grade in this activity will be based on the accuracy of your modeling and your seriousness of purpose in the estimation of your instructor(s).

At your station you should have:

- A cell cycle wheel
- A large Ziploc bag with materials
- Scissors/Tape
- Dried lima beans

1. First, become familiar with the chromosomes that will be used in your cell model. Your cell has 2 pairs of chromosomes. These contain letters representing genes. The paternal chromosomes have black genes, while the maternal chromosomes have pink colored genes.
   - Each pair is the same length. Find the 2 pairs. Throughout this simulation, each person in the group will be responsible for one of the chromosomes.
     - Each pair of chromosomes is made up of 2 partners, a maternal chromosome and a paternal chromosome.




DNA coiled around histone proteins

During this simulation, how would you tell the difference between the maternal and paternal chromosomes?

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2. The chromosomes are found inside your cell that is represented by the small Ziploc bag labeled "CELL". Place your 2 pairs of chromosomes into the small Ziploc bag. The remainder of the materials will be used throughout the activity and should be kept in the large bag labeled "MATERIALS", as a supply/synthesis area.

3. Let's Begin Mitosis! A cell next to your cell has died. This cell's death causes an **external growth signal** and tells your cell to begin the cell cycle.

Cell death acts as an external growth signal that stimulates cell division.

4. Turn your wheel to the **$G_1$ phase**. This is the growth phase. According to the cell cycle chart (from Part 1), what should happen during **$G_1$ phase?**

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5. To simulate growth of your cell, beans will be added to your small bag to represent an increase in the mass of your cell. Please add beans one at a time to your cell until the number of beans has doubled.

6. Turn your wheel until you reach the first checkpoint ( ). At this checkpoint, a growth regulator protein, called **Ras cyclin,** checks that cells are big enough to enter the next part of the cell cycle.
   - **Ras cyclin** is a protein that functions during this checkpoint. As the cell grows, the amount of **Ras cyclin** increases. When the amount of **Ras cyclin** reaches a certain level, it signals the cell to proceed to the next part of the cycle. Raise your hand so that **Ras cyclin** (your teacher) may check the mass of your cell.
   - If **Ras cyclin** does not give cells the signal to continue, the cells remain in this part of the cycle and continue to grow.

- Why is it important to check that the cell is big enough to continue with the cell cycle?

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- Once you have been given the signal to continue, proceed to step 7.

**Thought question**

- You have a mutation in the gene that produces the **Ras protein** and this checkpoint does <u>not</u> work. Do NOT check the mass of your cell. How might a malfunction at this checkpoint affect the cell?

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7. Before your cell is allowed to enter the next part of the cell cycle, it must pass a second checkpoint. Turn your wheel to the next checkpoint ( ).
   - DNA in these chromosomes can be damaged by a number of agents including radiation, toxic chemicals, and free radicals. At this checkpoint, another protein known as **p53** will inspect the chromosomes' DNA for damage. If there is DNA damage, **p53** will stop the cell cycle until DNA repair enzymes can fix the damage. If the DNA damage can't be repaired, **p53** may signal programmed cell death, called apoptosis.
   - Raise your hand to have **p53** (your teacher) check your DNA for damage.

   Imagine your cell has been exposed to excessive UV radiation (sunlight or tanning bed). This radiation causes DNA damage so part of your chromosome is missing. You have a mutation in the gene that produces the **P53 protein**. Because of this mutation, there is no checkpoint , and the cell can proceed with the cell cycle even though this DNA damage has occurred. How might a malfunction at this checkpoint affect the cell?

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8. If your cell has cleared the two checkpoints (that is, it is large enough and has suffered no DNA damage), turn your wheel to the **S phase** of the cell cycle. During this part of the cell cycle, DNA must be replicated. You must complete the following steps in order to replicate your DNA:

- Using the materials from the supply bag, (pencils, paper strips, scissors, small white rings) **make *exact* copies of each of your DNA strands.**
- These two copies (chromatids) are held together at the centromere region. Place the centromere regions of the chromatids on top of each other to simulate how the chromatids are held together.
- Summarize the events that occur during the S phase of the cell cycle

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9. Turn your wheel to the next checkpoint (  ). At this checkpoint, another protein complex called **ATM/Nibrin** inspects to make sure that the DNA was copied without mistakes.
   - Raise your hand to have **ATM/Nibrin** (your teacher) check your replicated DNA for damage.
   - Why is it important to check the replicated DNA?

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Imagine you had a mutation in the gene that produces the **ATM/Nibrin protein**. This would allow you to proceed to the next step of the cell cycle without inspecting to see if your DNA in your chromosomes was copied without damage.

How might a malfunction at this checkpoint affect the cell?

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10. Once you have been given the 'go ahead' to continue, turn your wheel and enter the **$G_2$** part of the cell cycle. During this part of the cell cycle, the cell prepares for mitosis by synthesizing the materials it will need. Please prepare your cell for mitosis by assembling the following materials:
    - Spindle apparatus (2 lanyard sets and paper clips). Pull black/white lanyard out of large bag. Notice that paper clip hooks are attached to the ends of the lanyard.

G1, S, and G2 of Interphase used to be called the "resting phase". Why is resting phase not a good name?

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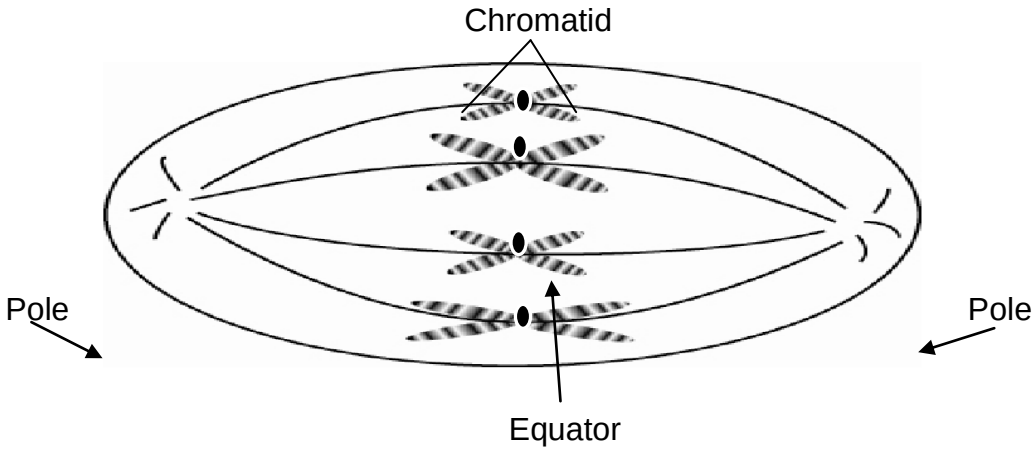
11. Move your wheel to the next part of the cell cycle, **Mitosis.** Proceed with mitosis by completing the following steps

- During **Prophase,** DNA in the chromosomes condenses and coils. To simulate this process, wrap each chromatid around a pencil and then remove the pencil. Attach your two coiled chromatids together by placing the centromeres on top of each other. These attachment sites now represent the centromere region.
- During **Metaphase,** the chromosomes line up in the center of the cell. Line up your chromosomes in the middle of your cell.




- Place one set of spindle fibers at each side (pole) of your desk (cell).
- Next, attach one spindle fiber from the left side of your desk to the centromere on one chromatid. Attach a spindle fiber from the right side of your desk to the centromere on the other chromatid. Poking the paper clip through the black region inside the white reinforcement makes these attachments.

12. Turn your wheel to the next checkpoint (  ). At this checkpoint another protein called **MAD1** checks to be sure that the spindle fibers have attached properly. Spindle fibers need to be attached correctly so that when the spindle fibers pull on the centromeres, the chromosomes are equally distributed to the new cells. Raise your hand to have **Mad1** (your teacher), check your spindle attachment.

13. If **MAD1** recognizes proper spindle attachment, your cell may proceed to **Anaphase** by pulling on the spindle apparatus to separate chromatids at the centromere.

    OH NO! Imagine you have a faulty spindle apparatus. One of the spindle fibers fails to attach to the centromere. In addition, you have a mutation in the gene that produces the **Mad1 protein**. There is no checkpoint! .

    - What problems may occur as a result of having a mutation at the **Mad1** checkpoint (  )?

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14. Remember that process of mitosis occurs in a cell. Complete **Telophase** by removing the spindle from the chromosomes. Place the spindle fibers back in the supply bag. Turn your wheel to next phase.

15. **Cytokinesis**: You may now divide your cell in half. Cut your small Ziploc bag, labeled "CELL" in half. You should now have two smaller baggies. Place the chromosomes from the left side of your desk into one half of the bag, and the chromosomes from the right side of your desk in the other half. Tape the open ends closed. You should now have two smaller cells.

    - Compare the chromosome content of the two cells.

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16. Each of these new cells would now enter $G_1$ phase and repeat the cell cycle.

**Analysis Questions:**

1. Why must replication occur in mitosis?

2. Explain the consequences of replication occurring without a subsequent cytokinesis (cell cytoplasm division).

3. Explain why embryonic cells are often selected for study of mitosis.

4. The nerve cells in humans seldom undergo mitosis. Based on this information, explain why complete recovery from injuries to the nervous system may not occur.

5-8. Discuss the importance of each of the four checkpoints we studied in this simulation of the cell cycle.

9. What is the relationship between the cell cycle and cancer?

10. Over half of all sporadic (random, non-hereditary) cancers have a mutation in the P53 gene. Why do you think a mutation in the p53 gene leads to so many cancers?